

Amendments to the Claims

Claim 1-24 (Cancelled)

Claim 25 (Currently Amended): A hybrid PKS gene assembly according to claim ~~68~~ 63 wherein said loading module is capable of loading a substrate to produce a starter unit different from a starter unit normally associated with said ~~at least one extension module~~ second Type I PKS.

Claim 26 (Cancelled)

Claim 27 (Currently Amended): A hybrid PKS gene according to claim ~~69~~ 25, wherein said loading module is the loading module of the avermectin-producing PKS of Streptomyces avermitilis.

Claims 28-30 (Cancelled)

Claim 31 (Currently Amended): A nucleic acid comprising ~~sequence encoding~~ a gene assembly according to claim ~~67~~ 63 operably linked to a PKS type II promoter.

Claim 32 (Currently Amended): A nucleic acid ~~sequence~~ according to claim 31, further comprising the natural activator gene for said promoter.

Claim 33 (Previously Presented): A nucleic acid according to claim 31, wherein the promoter is the act I promoter of S. coelicolor.

Claim 34 (Previously Presented): A nucleic acid according to claim 32, wherein the promoter is the act I promoter of S. coelicolor.

Claim 35 (Currently Amended): A hybrid polyketide synthase as

encoded by a gene assembly according to claim ~~67~~ 63.

Claim 36 (Currently Amended): A vector including a gene assembly according to claim ~~67~~ 63.

Claim 37 (Currently Amended): A transformed microorganism containing a gene assembly according to claim ~~67~~ 63 and able to express a polyketide synthase encoded thereby.

Claim 38 (Cancelled)

Claim 39 (Previously Presented): A method of making a polyketide by culturing the microorganism of claim 37 wherein said microorganism is an actinomycete selected from the group consisting of: *Saccharopolyspora erythraea*, *Streptomyces coelicolor*, *Streptomyces avermitilis*, *Streptomyces griseofuscus*, *Streptomyces cinnamomensis*, *Micromonospora griseorubida*, *Streptomyces hygroscopicus*, *Streptomyces fradiae*, *Streptomyces longisporoflavus*, *Streptomyces lasaliensis*, *Streptomyces tsukubaensis*, *Streptomyces griseus*, *Streptomyces venezuelae*, *Streptomyces antibioticus*, *Streptomyces lividans*, *Streptomyces rimosus* and *Streptomyces albus*.

Claims 40-43 (Cancelled)

Claim 44 (Currently Amended): A hybrid PKS gene assembly according to claim ~~67~~ 63, wherein said first nucleic acid portion ~~encodes encoding at least~~ a loading module and the adjacent KS1 domain which comprises an acyltransferase and an acyl carrier protein, ~~and said second nucleic acid portion encodes at least one extension module.~~

Claim 45 (Cancelled)

Claim 46 (Cancelled)

Claim 47 (Currently Amended): A plasmid comprising a gene assembly according to claim ~~67~~ 63.

Claim 48 (Previously Presented): A microorganism which has been transformed so that it harbors a plasmid according to claim 47.

Claim 49 (Previously Presented): A transformant microorganism according to claim 48 in which said plasmid replicates autonomously.

Claim 50 (Currently Amended): A plasmid comprising a gene assembly according to claim ~~67~~ 63 which is adapted to integrate into a specific attachment site (att) of a host's chromosome.

Claim 51 (Currently Amended): A method of producing a transformant microorganism comprising the steps of:

- (a) producing a plasmid which comprises donor DNA which is a gene assembly according to claim ~~67~~ 63, and
- (b) transforming with said plasmid a microorganism having a chromosome including DNA which undergoes homologous recombination with said plasmid to integrate said gene into the chromosome.

Claim 52-55 (Cancelled)

Claim 56 (Currently Amended): A transformed microorganism which naturally expresses a polyketide synthase and which contains as a result of its transformation a gene assembly according to claim ~~67~~ 63 and is operable to express a

polyketide synthase encoded thereby.

Claim 57 (Cancelled)

Claim 58 (Previously Presented): A method of making a polyketide by culturing the microorganism of claim 56, wherein said transformed prokaryotic organism is selected from the group consisting of: *Saccharopolyspora erythraea*, *Streptomyces coelicolor*, *Streptomyces avermitilis*, *Streptomyces griseofuscus*, *Streptomyces cinnamonensis*, *Micromonospora griseorubida*, *Streptomyces hygroscopicus*, *Streptomyces fradiae*, *Streptomyces longisporoflavus*, *Streptomyces lasaliensis*, *Streptomyces tsukubaensis*, *Streptomyces griseus*, *Streptomyces venezuelae*, *Streptomyces antibioticus*, *Streptomyces lividans*, *Streptomyces rimosus* and *Streptomyces albus*.

Claim 59 (Cancelled)

Claim 60 (Cancelled)

Claim 61 (Currently Amended): A hybrid polyketide synthase ("PKS") gene assembly encoding a functional polyketide synthase comprising a plurality of modules in which a DNA portion encoding a combinatorial module has been replaced by a DNA portion encoding at least one equivalent heterologous combinatorial module, said combinatorial module being a contiguous polypeptide sequence extending from a first point in ~~one~~ a first natural module to a second point at the corresponding position in ~~the next~~ a second natural module.

Claim 62 (Currently Amended): A hybrid polyketide synthase ("PKS") gene assembly encoding a functional polyketide synthase produced by

(a) providing a first nucleic acid portion encoding a plurality of modules of a first Type I PKS including a first extension module which produces a first ketide unit ~~of a first type~~; and

(b) replacing the nucleic acid encoding said first extension module with a second nucleic acid portion encoding a second extension module which is effective to produce a second ketide unit ~~of a second type~~, differing from said first ~~type~~ ketide unit in at least one of the characteristics selected from the group consisting of oxidation state, stereochemistry and substitution pattern.

Claim 63 (Currently Amended): A hybrid polyketide synthase (PKS) gene assembly encoding a functional polyketide synthase, said gene assembly comprising:

(a) a first nucleic acid portion of a first Type I PKS, said portion encoding a loading module and adjacent KS1 domain; and

(b) a second nucleic acid portion of a second Type I PKS comprising nucleic acid encoding a partial extension module which lacks a KS domain, so that the hybrid PKS gene encodes a hybrid extension module consisting of said KS domain of the first nucleic acid portion and said partial extension module.

Claim 64 (Currently Amended): A method of making a polyketide comprising:

(a) providing a transformed host microorganism selected from the group consisting of: *Saccharopolyspora erythraea*, ~~*Streptomyces coelicolor*~~, *Streptomyces avermitilis*, *Streptomyces griseofuscus*, *Streptomyces cinnamonensis*, *Micromonospora griseorubida*, *Streptomyces hygrosopicus*, *Streptomyces fradiae*, *Streptomyces longisporoflavus*, *Streptomyces lasaliensis*, *Streptomyces tsukubaensis*, *Streptomyces griseus*, *Streptomyces venezuelae*, *Streptomyces*

antibioticus, Streptomyces lividans, Streptomyces rimosus and Streptomyces albus containing a gene assembly according to claim ~~67~~ 63 operably linked to the act I promoter of *S. coelicolor*, ~~said host being a microorganism other than *S. coelicolor*~~; and

(b) culturing said transformed host microorganism to effect synthesis of said polyketide.

Claim 65 (Previously Presented): The method of claim 64, wherein said host microorganism also contains the act II - orf 4 activator of *S. coelicolor*.

Claim 66 (Previously Presented): The method of claim 65, wherein said transformed host microorganism is *S. erythraea*.

Claim 67-69 (Cancelled)

Claim 70 (Currently Amended): A hybrid polyketide synthase gene assembly according to claim ~~69~~ 63, wherein said loading module is selected from the group consisting of the loading modules of the rapamycin, FK506, and ascomycin-producing polyketide synthases.